REMARKS

The specification has been amended for clarification. The paragraph on page 14 mixes designation of the substituent on the hydroxyl group with the name of the resulting substituted hydroxyl. In order to be consistent, "carbonyl" has been changed to "carboxyl" since alkanoyl is used to describe the group earlier in this paragraph. Thus, the substituent is an aromatic or heterocyclic carbonyl or is pyrimidine carbonyl; the resulting group is an aromatic or heterocyclic carboxyl or a pyridine carboxyl, equivalent terminology to "benzoyl" and "acetyl," etc. This is for clarification only and no new matter has been added. Claims 1, 55 and 102 have been amended simply for clarification as is further described in response to the rejection under 35 U.S.C. § 112, paragraph 2.

The claims have been amended for clarification as requested by the Office. In addition, new claims 119-132 have been proposed for those embodiments of the invention wherein W is nitrogen. It is believed that these claims are clearly free of the cited art. No new matter has been added and entry of the amendment is respectfully requested.

The Rejections Under 35 U.S.C. § 112, Paragraph 2

All claims were rejected under this section due to an asserted lack of clarity. It is believed that the amendments to the claims and specification provide adequate clarification. In response to the specific criticisms made by the Office, applicants note the following. The numbers correspond to those in the Office action.

1. The point of the Office is well taken. The claims have been amended to provide that n'' is equal to 1 or 2; the Office is correct that if n'' were 0, this would be equivalent to V as a chemical bond.

2. A sulfonyl group need not be substituted and claim 1 has been reworded to clarify that the sulfonyl group does not have optional substitution.

3. The terminology C_{0-6} alkyl and C_{0-6} alkylamino is a shorthand version for what was intended. This is that when the alkyl group has 0 carbons, the named substituent is directly

connected to the remainder of the molecule. This has been clarified in the claims; rather than a C_{0-6} alkyl group substituted with an optionally substituted aromatic or heterocyclic group, the claim now reads on either an optionally substituted aromatic or heterocyclic group or a C_{1-6} alkyl group substituted with this; similarly, a C_{0-6} alkylamino group has been replaced by the alternatives of an optionally substituted amino group or an optionally substituted C_{1-6} alkylamino group. It is believed that the amendment says the very same thing that was intended by the original claim and thus no new matter has been added.

Applicants note there is a similar criticism in claim 51; it is assumed that claim 55 is intended and this claim has been amended in a corresponding manner.

4. It is believed that the correction to the specification obviates the confusion concerning "optionally substituted hydroxyl"; indeed, the substituent can include both alkyl groups and carbonyl groups. It is believed that the definitions in the specification are now consistent. The alkyl groups and carbonyl groups are the substituents; the resulting substituted hydroxyl is either an alkoxy or a carboxy moiety.

5. The criticism of claim 98 does not, in applicants' view, warrant an amendment. The code name and the name of the compound represent the same chemical structure. The code name is supplied to facilitate correlation of the structure with the name.

6. Claim 102 has been amended for clarification. As the compound of claim 1 already includes the acid addition salts and all the stereoisomeric possibilities, this phrase seems unnecessary; the addition of a pharmaceutically acceptable excipient responds to the rejection.

In light of the above, it is believed that the rejections under 35 U.S.C. § 112, paragraph 2, may be withdrawn.

The Rejection Under 35 U.S.C. § 103

Claims 1-2, 7 and 102 were rejected as assertedly obvious over Bowles, *et al.* It is noted with appreciation that claims 3-4, 6, 12-13, 51, 55-58 and 98 are free of this rejection. It is also believed that new claims 119-133 are free of this rejection since no compounds in the Bowles

document refer to any compounds where the complex system "X" is linked to a nitrogen atom. Accordingly, only claims 1-2, 7 and 102, in respect of those embodiments where W is a carbon atom need be addressed.

It appears the Office is correct that the very large genus described by Bowles theoretically includes, at some level, the very different set of compounds claimed in the instance wherein W is a carbon atom. However, it seems clear to applicants that Bowles does not suggest the specific genus required by the claims. Applicants are appreciative that the Office itself recognizes this, in that all of the exemplified compounds in Bowles require the presence of CO or SO_2 as Bowles' embodiment of Q. It is true that Bowles recognizes that Q may be a bond and indeed, in column 13, indicates how a compound could be synthesized when Q is a bond. However, this does not demonstrate that a carbonyl group or an SO_2 group and a bond are, in fact, equivalent. It is certainly the case that Bowles does not point the reader toward the set of compounds required by the present claims.

It is well established that a genus which includes a species does not necessarily defeat patentability of a claim to that species if that species is not suggested by the cited document. (*In re Jones*, 958 F2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992); and *In re Baird*, 16 F3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994).) That is precisely the situation here. First, as long as Q represents carbonyl, thiocarbonyl or a sulfonyl group, Bowles teaches away from the compounds of the present claims. It is noted that, although Bowles includes in its generic description the possibility that Q represents a bond, the issued claims are limited to instances where Q is carbonyl, thiocarbonyl or sulfonyl. Either the Office made the decision that these were separate inventions and thus restricted-out the instance where Q represented a bond (in which case a patentable distinction has been acknowledged by the Office) or the Office considered that Bowles so taught away from the embodiment where Q is a bond that that embodiment was not included in the allowed claim. In either instance, the fate of this broader disclosure in the granted claims indicates that there is no equivalence from a patent standpoint between Q as a bond and Q as a carbonyl, thiocarbonyl or sulfonyl.

Second, and over and above this, although the present claims require that R^8 be an optionally substituted heterocyclic group or optionally substituted aromatic group, Bowles teaches away from this as well. None of the exemplified compounds contain such a group. Most of the exemplified compounds are those where "B" contains an oxygen atom and does not contain a heterocycle or other cyclic group. These possibilities are listed, but taught away from by the exemplified compounds.

Thus, since the disclosure of Bowles focuses the reader away from the claimed subject matter, on this basis alone, the disclosure of Bowles does not render the present claims 1-2, 7 or 102 obvious.

In addition, consideration of the biological and pharmacological properties of the compounds should be taken into account. *In re Papesch*, 315 F2d 381, 137 USPQ 43 (CCPA 1963). In addition to the reasons cited above for finding a distinction between with compounds of Bowles and the compounds of the present invention, it should be noted that the compounds of the present invention are disclosed as agents that modulate chemokine receptor activity. According to Stedman's Medical Dictionary, 27th ed., Lippincott Williams & Wilkins (2000), chemokines are defined as "Groups composed of usually 8-10 kD polypeptide cytokines that are chemokinetic and chemotactic in stimulating leukocyte movement and attraction." Thus, compounds, which are cytokines interact with receptors residing on leukocytes as further defined in the specification at pages 7-8, bridging paragraph. On the other hand, the Bowles compounds are not disclosed to have these activities; rather they are antagonists of platelet activating factor (PAF) which is not a cytokine. It is a bioactive phospholipid which may have chemokinetic activity, but is not a "cytokine" as defined in the art. Thus, in addition to their clear structural non-obviousness, the compounds of the invention possess a property not disclosed in the art. The invention, then, taken as a whole is patentable on this basis as well.

CONCLUSION

Applicants have amended the claims to overcome any rejections under 35 U.S.C. § 112, paragraph 2. Applicants appreciate that claims 3-4, 6, 12-13, 51, 55-58 and 98 are free of the art; applicants believe that new claims 119-132 are free of the art as well. The claims rejected over Bowles, claims 1-2, 7 and 102 are, in fact, not rendered obvious since Bowles teaches away from the set of claimed compounds, which fail to contain what appears to be a vastly preferred group, CO, or SO_2 between any aryl linking group (itself a rare occurrence in the examples) and the required nitrogen. In addition, the Bowles compounds are not disclosed as having cytokine activity. Accordingly, it is believed that the pending claims, claims 1-4, 6-7, 12-13, 51, 55-58, 98, 102 and 119-132 are in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 391442003700.

Respectfully submitted,

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EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

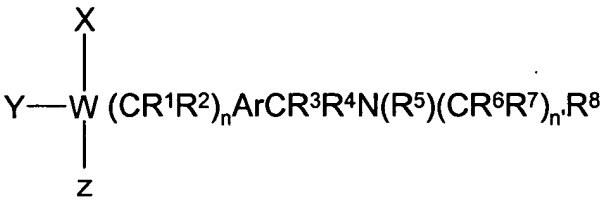
In the Specification:

Please amend the paragraph on page 14, lines 3-6 as follows:

Further examples of the optionally substituted hydroxyl group include an optionally substituted C_{2-4}alkanoyl (e.g. acetyl, propionyl, butyryl, isobutyryl, etc.), C_{1-4} [alkylsufonyl] alkylsulfonyl (e.g. methanesulfonyl, ethanesulfonyl, etc.) and an optionally substituted aromatic and heterocyclic [carbonyl] carboxyl group including benzoyl, [pyridinecarbonyl] pyridinecarboxyl, etc.

In the Claims:

1. (Four times amended) A compound according to Formula I:



(I)

wherein, W is a nitrogen atom and Y is void or, W is a carbon atom and Y=H;

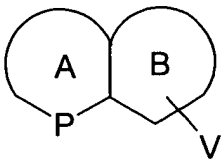
R^1 to R^7 may be the same or different and are independently hydrogen or straight, branched or cyclic C_{1-6} alkyl;

R^8 is an optionally substituted heterocyclic group or an optionally substituted aromatic group

Ar is an aromatic or heteroaromatic ring optionally substituted at single or multiple, non-linking positions with electron-donating or withdrawing groups;

n and n' are independently, 0-2;

X is a group of the formula:



wherein, Ring A is an optionally substituted, saturated or unsaturated 5 or 6-membered ring, and P is an optionally substituted nitrogen atom and wherein any heteroatom in ring A or B is N;

wherein Ring B is an optionally substituted 5 to 7-membered ring;

wherein Ring A or Ring B is bound to group W from any position through group V;

wherein V is a chemical bond or V is a $(CH_2)_{n''}$ group (where [n''= 0-2] n''= 1-2), or V is a C=O group; and

wherein Z is selected from the group consisting of: a hydrogen atom; an optionally substituted C_{1-6} alkyl group; an optionally substituted aromatic or heterocyclic group; a [C_{0-6}] C_{1-6} alkyl group substituted with an optionally substituted aromatic or heterocyclic group; an optionally substituted amino group; an optionally substituted [C_{0-6}] C_{1-6} alkylamino or C_{3-7} cycloalkylamino group; a sulfonyl group and an optionally substituted carbonyl group [or sulfonyl]; and the pharmaceutically acceptable acid addition salts thereof; and

any stereoisomeric forms and mixtures of stereoisomeric forms thereof.

55. (Amended) The compound of claim 1, wherein Z is an optionally substituted aromatic or heterocyclic group or a [C_{0-6}] C_{1-6} alkyl group optionally substituted with an optionally substituted [fused or unfused,] aromatic or heterocyclic group.

102. (Twice amended) A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 1 in admixture with at least one pharmaceutically acceptable excipient[; wherein said composition further comprises any pharmaceutically acceptable acid addition salts thereof and any stereoisomeric forms and mixtures of stereoisomeric forms thereof].